

### ***Remarks***

#### **I. Status of the Claims**

Claims 1-179, 181-182, 190-191, 193-194, 212-213, 215-216, 241, 250, 254, 275-277, and 279 are canceled. Applicants reserve the right to claim the subject matter of the canceled claims in continuing applications. Claims 176-177, 180, 183-189, 192, 195-201, 204-211, 214, 217-223, 226-240, 243-249, 251-253, 255-265, 268-274, 278, and 280-282 are pending in the application, with claims 176, 210, 232, 249, 251, 253, 255, 263, 274, 278, and 280 being the independent claims.

#### **II. Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph**

Claims 176-177, 180, 183-189, 192, 195-201, 204-214, 217-223, 226-240, 243-249, 251-253, 255-265, 268-274, 276, 278 and 280-282 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. (Office Action, page 2.) Applicants respectfully disagree but have amended claims to facilitate prosecution.

The Examiner asserts that the phrase “capable of preventing differentiation” is indefinite because “[i]t is unclear whether these characteristics actually occur or that the medium could potentially prevent differentiation.” (Office Action, page 2.) Solely to advance prosecution, and not in acquiescence to the Examiner’s rejection, Applicants have amended the independent claims to recite “prevents” differentiation. Applicants believe that these amendments address the Examiners concerns and respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph.

#### **III. Rejection of the Claims Under 35 U.S.C. § 103(a)**

Claims 176-177, 180, 183-189, 192, 195-201, 204-214, 217-223, 226-240, 243-249, 251-253, 255-265, 268-274, 276, 278 and 280-282 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ponting (U.S. Patent No. 5,405,772), GIBCO BRL Products and Reference Guide (1997) Chapters 5 and 8 (referred to hereafter as “the GIBCO reference”) and Atsumi *et al.* (*Develop. Growth & Differ.* 35:81-87 (1993)). (Office Action, page 4.)

Claims 176-177, 180, 183-189, 192, 195-201, 204-214, 217-223, 226-240, 243-249, 251-253, 255-265, 268-274, 276, 278 and 280-282 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ponting, the GIBCO reference, Atsumi *et al.* and Nichols *et al.* (*Exp. Cell Res.* 215:237-239 (1994)). (Office Action, page 7.)

Applicants respectfully disagree with the above rejections.

The Examiner asserts that by combining the disclosures of Ponting, Atsumi *et al.*, Nichols *et al.* and the Gibco reference, one of skill in the art would arrive at the presently claimed invention. (Office Action, pages 4 and 7.) The U.S. Supreme Court recently noted that:

A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, *it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.* This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

(*KSR Int'l v. Teleflex Inc.*, 550 U.S. at \_\_, Slip Op. at 1-24 (Apr. 30, 2007) (No. 04-1350) (emphasis added).) Thus, the U.S. Supreme Court has provided guidance for assessing whether an invention is obvious and has indicated that merely collecting “building blocks” does not provide a reason that would prompt one of skill in the art to arrive at the claimed invention.

Applicants believe this rejection under 35 U.S.C. § 103(a), as applied to the claims presented herein, is improper because: 1) not all elements of the claims are taught by the cited references; and 2) at the time of filing, there was no motivation or suggestion to combine the elements of the present claims in the manner claimed.

With regards to above, the claims as presented herein refer to, *inter alia*, serum-free cell culture media or supplements which prevent differentiation of mouse embryonic stem cells during expansion and none of the cited references disclose these elements. For example, Ponting focuses on methods and compositions for the culture of hematopoietic cells, not embryonic stem cells. In fact, Applicants have found only one sentence in Ponting which refers to embryonic stem cell lines. (Ponting, column 9, lines 9-14.) This sentence states that “[t]he culture media also supports a wide range of cell lines including immortalized versions of those already listed;

examples of others include . . . embryonic stem cell lines". (Ponting, column 9, lines 9-14.) Applicants have found no disclosure in Ponting teaching that the cell culture medium discussed in Ponting prevents differentiation of mouse embryonic stem cells during expansion. Actually, Ponting notes that hematopoietic stem cells undergo hematopoiesis when cultured in the serum free medium discussed therein. For example, Ponting states "[i]t was determined that only the medium of the current invention showed any signs of hematopoiesis taking place". (Ponting, column 17, lines 63-65.) Therefore, Ponting neither teaches nor suggests cell culture media which prevents differentiation of hematopoietic cells or mouse embryonic stem cells. Further, Atsumi *et al.*, Nichols *et al.* and the GIBCO reference do not cure the deficiencies of Ponting. Nichols *et al.* relates to different technology from the claimed invention because it discloses methods of culturing stem cells in the presence of serum, not in serum free medium as in the present claims. (Office Action, page 10.) Since all elements of the present claims are neither taught nor suggested by the cited references, a *prima facie* case of obviousness has not been established.

The Examiner notes on page 9 of the Office Action that "these elements were commercially available at the time of filing of this application (for example page 15 of the instant specification) and also evidenced by the Gibco BRL Products and Guide." Applicants refer to the above cited Supreme Court case which specifically states that "[a] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Even if the cited references refer to components of the claimed invention, the references, alone or in combination, do not lead one skilled in the art to the claimed invention. In particular, the cited references do not teach or suggest methods for preventing differentiation of embryonic stem cells. Thus, there is no suggestion or motivation to combine elements to arrive at, *inter alia*, a serum-free cell culture medium which prevents differentiation of mouse embryonic stem cells during expansion, wherein the serum-free cell culture medium comprises a lipid-rich serum albumin and comprises at least one factor selected from the group consisting of a leukemia inhibiting factor, a steel factor, a ciliary neurotrophic factor and an oncostatin M.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 103(a).

***Conclusion***

Applicants believe that a full and complete Reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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